Remarks

I. Request for Continued Examination (RCE).

A Request for Continued Examination (RCE) accompanies this paper. The RCE is being filed after the final Office action, mailed 26 December 2006. Accordingly, applicant requests that the filing of the RCE is treated as a request to reopen prosecution of the application before the Examiner.

II. Addressing The Examiner's Rejections.

1. Rejection of Claims 2, 3, 8, 10, 14-17, 19, 22, 24, 30, 33, 35-38, 40-47, 49-54, 68-77 and 84-85 Under 35 U.S.C. §103(a).

The Examiner rejected claims 2, 3, 8, 10, 14-17, 19, 22, 24, 30, 33, 35-38, 40-47, 49-54, 68-77 and 84-85 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over "Sorenson" (U.S. Patent No. 5,207,752) in view of "Palmeri" (J. Chemotherapy 2(3):327-330 (1990)) and "Harper" (U.S. Patent No. 6,436,091).

Claims 2, 3, 8, 10, 14-17, 19, 35-38, 40-47, 49-54, 68-77 and 84-85 are canceled by the amendments set forth herein. Cancellation these claims is not intended to be an acquiescence in the Office's assessment of those claims in the final Office action, mailed 26 December 2006.

Accordingly, this rejection is moot and withdrawal thereof is respectfully requested.

2. Rejection of Claims 3-7, 12, 13, 19, 20, 22, 24-27, 29, 32, 33, 68, 74, 78-83 and 86-88 Under 35 U.S.C. §103(a).

The Examiner rejected claims 3-7, 12, 13, 19, 20, 22, 24-27, 29, 32, 33, 68, 74, 78-83 and 86-88 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over "Sorenson" (U.S. Patent No. 5,207,752) in view of "Palmeri" (J. Chemotherapy 2(3):327-330 (1990)) and "Harper" (U.S. Patent No. 6,436,091) and further in view of "Johnson" (Scientific American, May 1994, pages 68-75).

Claims 3-7, 12, 13, 19, 20, 22, 24-27, 29, 32, 33, 68, 74, and 78-83 are canceled by the amendments set forth herein. Cancellation these claims is not intended to be an

acquiescence in the Office's assessment of those claims in the final Office action, mailed 26 December 2006. Accordingly, the rejection of these claims is moot and only the rejection of claims 86-88 is addressed herein below.

In *KSR Int'l Co. v. Teleflex Inc.,* 127 S. Ct. 1727; 167 L. Ed. 2d 705; 2007 U.S. LEXIS 4745; 75 U.S.L.W. 4289; 82 USPQ.2D 1385 (S.Ct. 2007), the Supreme Court reaffirmed use of the Graham factors in the determination of obviousness under 35 U.S.C. § 103(a). The four factual inquiries under Graham are: (a) determining the scope and contents of the prior art; (b) ascertaining the differences between the prior art and the claims in issue; (c) resolving the level of ordinary skill in the pertinent art; and (d) evaluating evidence of secondary consideration. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 86 S. Ct. 684, 15 L. Ed. 2d 545, 148 USPQ 459, 467 (S.Ct. 1966).

All of the pending claims in the present application at least contain the limitations presented in independent claim 86, as follows:

> 86. A method of treating hepatitis C (HCV) in a subject in need of such treatment, comprising
> administering a therapeutically effective amount of omega interferon protein to the subject.

Accordingly, all of the pending claims distinguish over the cited references at least for the reasons discussed herein below relative to limitations present in independent claim 86.

In view of the four factual inquires under Graham, applicant submits that the Office has failed to establish a case of *prima facie* obviousness for the following reasons.

In determining the scope and content of the cited prior art, the primary reference of "Sorenson" (U.S. Patent No. 5,207,752) contains teachings directed to a two-stage iontophoretic drug delivery system. The iontophoretic system provides that iontophoretic current is delivered at a first level for a first predetermined interval to rapidly introduce a therapeutic agent into the bloodstream and thereafter reduced to a second lower level to maintain a desired steady-state therapeutic level of the agent (see, e.g., Abstract). The reference contains only a generic teaching regarding anti-viral therapeutic agents (see, col. 6, lines 26-29). The reference contains only a generic teaching regarding "interferon" which is contained in a laundry list of peptides and proteins (see, col. 6, line 50, to col. 7, line 15).

Regarding the differences between the prior art and the claims in issue, neither use of

omega interferon protein nor treatment of hepatitis (in particular, hepatitis C) is taught in the "Sorenson" reference. Accordingly, the reference of "Sorenson" does not even teach the elements of the claimed invention.

In determining the scope and content of the cited prior art, the secondary reference of "Palmeri" (J. Chemotherapy **2**(3):327-330 (1990)) contains teachings directed to the use of 5-fluorouracil and recombinant alpha interferon-2a in the treatment of advanced colorectal carcinoma. The reference generally describes a dose optimization study with the aim of identifying the maximally tolerated dose of recombinant alpha intereron-2a in combination with 5-fluorouracil (see, e.g., Abstract).

Regarding the differences between the prior art and the claims in issue, neither use of omega interferon protein nor treatment of hepatitis (in particular, hepatitis C) is taught in the "Palmeri" reference. Accordingly, the reference of "Palmeri" does not even teach the elements of the claimed invention and thus fails to make up for the shortcomings of the primary reference.

In determining the scope and content of the cited prior art, the tertiary reference of "Harper" (U.S. Patent No. 6,436,091) contains teachings directed to implantable devices and osmotic pump and catheter systems for delivering a pharmaceutical agent to a patient at selectable rates (see, e.g., Abstract).

Regarding the differences between the prior art and the claims in issue, neither use of omega interferon protein nor treatment of hepatitis (in particular, hepatitis C) is taught in the "Harper" reference. Accordingly, the reference of "Harper" does not even teach the elements of the claimed invention and thus fails to make up for the shortcomings of the primary and secondary references.

In determining the scope and content of the cited prior art, the quaternary reference of "Johnson" (Scientific American, May 1994, pages 68-75) is a review article generally discussing how interferons fight disease. The most discussed interferons in the article are alpha interferon, beta interferon, and gamma interferon. The reference discusses the use of **alpha interferon only** for the treatment of chronic hepatitis C (see, page 74); but does not teach that any other interferon is useful for the treatment of chronic hepatitis C. Further, the reference contains only a mention of omega interferon -- indicating that it is classified as a

Type I interferon (see, page 70). The reference does not explicitly teach any therapeutic use for omega interferon. The reference teaches therapeutic uses for alpha interferon, beta interferon, and gamma interferon (see, e.g., pages 74 and 75). As noted in the specification of the present application: "[o]mega-IFN is a naturally occurring interferon which has limited homology to the alpha interferons (65%) and even less homology to the beta interferons (35%), i.e., omega interferon is structurally distinctive" (see, specification of the present application, ¶0053). Accordingly, there is no teaching in the "Johnson" reference that any interferon other than alpha interferon would be a useful therapeutic agent for the treatment of hepatitis C.

Regarding the differences between the prior art and the claims in issue, the reference of "Johnson" does not teach the use of omega interferon protein for treatment of hepatitis (in particular, hepatitis C). Accordingly, the reference of "Johnson" does not teach the elements of the claimed invention and thus fails to make up for the shortcomings of the primary, secondary, and tertiary references.

When resolving an obviousness issue, "the question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination." *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1462, 221 USPQ 481, 488 (Fed. Cir. 1984). Care must be taken to avoid hindsight reconstruction by using "the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit." *Orthopedic Equip. Co. v. United States*, 702 F.2d 1005, 1012, 217 USPQ 193, 199 (Fed. Cir. 1983). There is no teaching in the "Johnson" reference that would guide one of ordinary skill in the art to achieve the results of the claims in suit, that is, treatment of hepatitis C in a subject in need of treatment by administering a therapeutically effective amount of omega interferon protein.

Accordingly, applicant submits that the Examiner has failed to establish a case of *prima facie* obviousness for the presently claimed invention as none of the cited references teach treatment of hepatitis C in a subject in need of treatment by administering a therapeutically effective amount of omega interferon protein.

In view of the above-presented amendments to the claims and arguments, applicant

respectfully requests that the rejections under 35 U.S.C. §103 be withdrawn.

3. Rejection of Claims 2, 11, 22, 31, 68 and 74 Under 35 U.S.C. §103(a).

The Examiner rejected claims 2, 11, 22, 31, 68 and 74 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over "Sorenson" (U.S. Patent No. 5,207,752) in view of "Palmeri" (J. Chemotherapy **2**(3):327-330 (1990)), "Harper" (U.S. Patent No. 6,436,091) and "Johnson" (Scientific American, May 1994, pages 68-75) and further in view of "Kwan" (U.S. Patent No. 4,847,079).

Claims 2, 11, 22, 31, 68 and 74 are canceled by the amendments set forth herein. Cancellation these claims is not intended to be an acquiescence in the Office's assessment of those claims in the final Office action, mailed 26 December 2006.

Accordingly, this rejection is moot and withdrawal thereof is respectfully requested.

4. Rejection of Claims 2-17, 19, 20, 22, 24-27, 29-33, 35-38, 40-47, 49-54 and 68-88 Under 35 U.S.C. §103(a).

The Examiner rejected claims 2-17, 19, 20, 22, 24-27, 29-33, 35-38, 40-47, 49-54 and 68-88 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over "Sorenson" (U.S. Patent No. 5,207,752) in view of "Palmeri" (J. Chemotherapy **2**(3):327-330 (1990)), "Peery" (U.S. Patent No. 5,728,396), and "Johnson" (Scientific American, May 1994, pages 68-75) and further in view of "Kwan" (U.S. Patent No. 4,847,079).

Claims 2-17, 19, 20, 22, 24-27, 29-33, 35-38, 40-47, 49-54 and 68-85 are canceled by the amendments set forth herein. Cancellation these claims is not intended to be an acquiescence in the Office's assessment of those claims in the final Office action, mailed 26 December 2006. Accordingly, the rejection of these claims is moot and only the rejection of claims 86-88 is addressed herein below.

In *KSR Int'l Co. v. Teleflex Inc.,* 127 S. Ct. 1727; 167 L. Ed. 2d 705; 2007 U.S. LEXIS 4745; 75 U.S.L.W. 4289; 82 U.S.P.Q.2D 1385 (S.Ct. 2007), the Supreme Court reaffirmed use of the Graham factors in the determination of obviousness under 35 U.S.C. § 103(a). The four factual inquiries under Graham are: (a) determining the scope and contents

of the prior art; (b) ascertaining the differences between the prior art and the claims in issue; (c) resolving the level of ordinary skill in the pertinent art; and (d) evaluating evidence of secondary consideration. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 86 S. Ct. 684, 15 L. Ed. 2d 545, 148 USPQ 459, 467 (S. Ct. 1966).

All of the pending claims in the present application at least contain the limitations presented in independent claim 86, as follows:

> 86. A method of treating hepatitis C (HCV) in a subject in need of such treatment, comprising
> administering a therapeutically effective amount of omega interferon protein to the subject.

Accordingly, all of the pending claims distinguish over the cited references at least for the reasons discussed herein below relative to limitations present in independent claim 86.

In view of the four factual inquires under Graham, applicant submits that the Office has failed to establish a case of *prima facie* obviousness for the following reasons.

The shortcomings of the reference of "Sorenson" as the primary reference were discussed herein above. The failings of the references of "Palmeri" and "Johnson" were also discussed herein above.

In determining the scope and content of the cited prior art, the tertiary reference of "Peery" (U.S. Patent No. 5,728,396) contains teachings directed to sustained delivery of leuprolide using an implantable system. The reference contains a generic teaching regarding pharmacologically active agents including a long list of possibly useful peptides, including alpha, beta, and delta interferon (see, col. 11, lines 19-20). The reference also contains a generic teaching regarding possible use of active agents for the treatment of a variety of conditions. The reference includes a long list of conditions that might be treated, including hepatitis (see, col. 11, lines 28-38), though there is no connection presented suggesting which active agent would treat which condition.

Regarding the differences between the prior art and the claims in issue, neither use of omega interferon protein nor treatment of hepatitis C is taught in the "Peery" reference. Accordingly, the reference of "Peery" does not even teach the elements of the claimed invention and fails to make up for the shortcomings of the primary and secondary references.

In determining the scope and content of the cited prior art, the quinary reference of

"Kwan" (U.S. Patent No. 4,847,079) contains teachings directed to biologically stable interferon compositions comprising thimerosal (see, e.g., Abstract). The reference teaches that "the term 'interferon' includes natural and recombinant alpha (leucocyte) and beta (fibroblast) interferons, but alpha interferons are preferred" (see, e.g., col. 1, lines 26-28).

Regarding the differences between the prior art and the claims in issue, neither omega interferon protein nor treatment of hepatitis (in particular, hepatitis C) is taught in the "Kwan" reference. Accordingly, the reference of "Kwan" does not even teach the elements of the claimed invention and fails to make up for the shortcomings of the primary, secondary, tertiary, and quaternary references.

Accordingly, applicant submits that the Examiner has failed to establish a case of *prima facie* obviousness for the presently claimed invention as none of the cited references teach treatment of hepatitis C in a subject in need of treatment by administering a therapeutically effective amount of omega interferon protein.

In view of the above-presented amendments to the claims and arguments, applicant respectfully requests that the rejections under 35 U.S.C. §103 be withdrawn.

5. Rejection of Claim 68 Under 35 U.S.C. §112, second paragraph.

The Examiner rejected claim 68 under 35 U.S.C. §112, second paragraph, asserting that the claim is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner asserted that the limitation "said pharmacokinetic profile during said long-term delivery" on line 9 lacks sufficient antecedent basis for this limitation in the claim.

Claim 68 is canceled by the amendments set forth herein. Cancellation this claim is not intended to be an acquiescence in the Office's assessment of that claim in the final Office action, mailed 26 December 2006.

Accordingly, this rejection is moot and withdrawal thereof is respectfully requested.

III. Supplemental Information Disclosure Statement.

Accompanying this paper is a Supplemental Information Disclosure Statement.

Applicant requests that the Examiner indicate that the references have been considered and are of record by initialing each cited reference on the accompanying modified form 1449 and returning a copy of the initialed form to the applicant.

Conclusion

Applicant respectfully submits that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Please direct all future correspondences in connection with this application to:

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No additional fees are believed due in connection with this paper. However, the Commissioner is hereby authorized to charge to Deposit Account No. **504212** (please reference docket number **INT 004.10**) any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, with the exception of the payment of the Issue Fee.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact Barbara G. McClung, Esq., at (510) 652-2600 (ext. 296).

Respectfully submitted,

Date: 29 May 2007 By: _____

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AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph on page 1, line 5, with the following amended paragraph:

~~METHOD FOR SHORT-TERM AND LONG-TERM DOSIMETRY~~

METHOD FOR TREATING DISEASES WITH OMEGA INTERFERON

Please amend ¶0059, on page 17, lines 21-26 as follows:

[0059] In Figure 2, a graph is presented that shows an increase in the response rate as measured by complete viral clearance in human patients with chronic HCV infection previously untreated with an interferon. Each patient was treated short-term for various periods of time with ~~15 μg/dose~~ the dosages shown in Figure 2 of omega-IFN per week. ~~, with 7 doses per week for 2 weeks then~~ 3 doses were given per week on days 1, 3, and 5 of each 7 day week ~~thereafter..~~thereafter. The tolerability and safety profile is reasonably well established within 4 weeks after beginning treatment.

Please amend ¶00116, on page 34, lines 16-18 as follows:

[0116] In the case of viral hepatitis C, the preferred unit-dose per quarter-year is 300-8100 μg (i.e., about 23 to about 623 μg per week) of omega-IFN. A more preferred unit-dose per quarter-year is 300-5040 μg (i.e., about 23 to about 388 μg per week) and the most preferred unit-dose per quarter-year is 630-2520 μg (i.e., about 48 to about 194 μg per week).

AMENDMENTS TO THE CLAIMS

(including complete listing of the claims)

1-85. (Canceled)

86. (Currently Amended) A method of treating hepatitis C (HCV) in a subject in need of such treatment, comprising:

-administering ~~to~~ a therapeutically effective amount of omega interferon protein to the subject. ~~patient an amount of omega interferon effective to provide therapeutic benefit for at least 3 months, wherein the omega interferon is formulated in an implantable device that is not externally programmable that delivers the omega interferon at a constant rate for said at least 3 months.~~

87. (Currently Amended) A method of treating hepatitis C (HCV) in a subject in need of such treatment, comprising:

~~a) determining for a patient an amount of omega interferon that has a well-tolerated, therapeutic index for said patient; and~~

~~b)~~ administering a therapeutically effective amount of omega interferon protein to the subject, wherein (i) the omega interferon is administered at a controlled rate over time, and (ii) the therapeutically effective amount of omega interferon is an amount of omega interferon selected from the group consisting of between about 48 and about 194 micrograms per week, between about 23 and about 388 micrograms per week, and between about 23 and about 623 micrograms per week.

~~to said patient using one or more internally presented, not externally programmable pumps an amount of omega interferon effective to achieve said therapeutic index for a period of 3-12 months~~.

88. (Currently Amended) A method of treating hepatitis C (HCV) in a subject in need of such treatment, comprising:

~~a) determining for a patient an amount of omega interferon that has a well-tolerated,~~

~~pharmacokinetic profile for said patient; and~~

~~b)~~ administering a therapeutically effective amount of omega interferon protein to the subject, wherein (i) the omega interferon is administered by injection, and (ii) the therapeutically effective amount of omega interferon is an amount of omega interferon selected from the group consisting of between about 1 and about 210 micrograms per week and between about 22.5 and about 360 micrograms per week.~~to said patient using one or more internally presented, not externally programmable pumps an amount of omega interferon effective to achieve said pharmacokinetic profile for a period of 3-12 months.~~

89. (New) The method of claim 86, wherein the therapeutically effective amount of omega interferon is administered by injection.

90. (New) The method of claim 89, wherein the therapeutically effective amount of omega interferon is administered by one or more daily injections.

91. (New) The method of claim 89, wherein the therapeutically effective amount of omega interferon is administered by one or more injections given at selected dosing intervals.

92. (New) The method of claim 91, wherein the dosing interval comprises three injections per week.

93. (New) The method of claim 89, wherein the method of injection is selected from the group consisting of subcutaneous injection, intramuscular injection, and bolus intravenous injection.

94. (New) The method of claim 93, wherein the omega interferon is administered by subcutaneous injection.

95. (New) The method of claim 86, wherein the omega interferon is administered by

infusion.

96. (New) The method of claim 95, wherein the method of infusion is chronic intravascular infusion.

97. (New) The method of claim 86, wherein the omega interferon is administered at a controlled rate over time.

98. (New) The method of claim 97, wherein a device is used to administer the omega interferon.

99. (New) The method of claim 98, wherein the device comprises a pump.

100. (New) The method of claim 99, wherein the device is either implanted in or external to the subject.

101. (New) The method of claim 100, wherein the device is implanted.

102. (New) The method of claim 101, wherein the device comprises an osmotic pump.

103. (New) The method of claim 97, wherein two or more implantable devices are used to administer the omega interferon.

104. (New) The method of claim 86, wherein the therapeutically effective amount of omega interferon is between about 1 and about 210 micrograms per week.

105. (New) The method of claim 86, wherein the therapeutically effective amount of omega interferon is between about 22.5 and about 360 micrograms per week.

106. (New) The method of claim 86, wherein the therapeutically effective amount of omega interferon is between about 23 and about 623 micrograms per week.

107. (New) The method of claim 86, wherein the omega interferon is a recombinant omega interferon.

108. (New) An implantable device for use in the method of claim 102, the device comprising

an osmotic pump, and

a reservoir comprising omega interferon.

109. (New) A kit comprising two or more implantable devices for use in the method of claim 103, wherein the kit comprises at least a first device and a second device, wherein the amount of omega interferon in the first device is less than the amount of omega interferon in the second device.

110. (New) The kit of claim 109, wherein the first device comprises a fractional unit-dose of omega interferon and the second device comprises a unit-dose of omega interferon.

111. (New) The kit of claim 110, wherein the kit comprises one or more of the first device and one or more of the second device.

112. (New) A method of manufacturing the kit of claim 109, comprising

preparing a first device comprising a fractional unit-dose of omega interferon, and

preparing a second device comprises a unit-dose of omega interferon.

113. (New) The method of manufacturing of claim 112, further comprising combining one or more first device with one or more second device in a kit.